disclose to be a condition dependent upon cancer. Applicants respectfully submit that the assumptions underlying this rejection are insufficiently supported.

Robbins Teaches Away From The Claimed Invention. Robbins suggests that TNF-alpha, IL-1, and/or IFN-gamma are responsible for mediating cancer cachexia (p. 295, left column). Therefore, one of ordinary skill following the teaching of the prior art would have been led in the direction of an anti-TNF, anti-IL-1, or anti-IFN antibody rather than an anti-IL-6R antibody. One certainly would not have expected to be able to treat cachexia with anti-IL-6R in view of the teachings of Robbins that "[o]ther cytokines, such as IL-1 and IFN-[gamma], synergize with TNF-[alpha], and the possibility exists that several soluble factors collaborate in contributing to malnutrition in cancer patients" (page 295, left column).

The References Collectively Fail To Teach One Of Ordinary Skill Whether An Anti-IL-6R Antibody Has A Strong Enough Effect On Cancer Such That It Would Reasonably Be Expected To Have An Effect On Cachexia. Suzuki, at best, establishes that certain anti-IL-6R antibodies can be used to "block myeloma cell proliferation *in vivo*" (p. 1999, right column) (emphasis supplied). Sato shows that reshaped anti-IL-6R antibody inhibits myeloma cell growth *in vitro*. Neither Suzuki nor Sato teach or suggest that anti-IL-6R antibody has an effect strong enough and early enough to have an appreciable impact on cachexia. The secondary references further establish this point. Though the secondary references do teach that cachexia results from cancer, the rejection fails to show any prior art teaching that cancer underlying cachexia can be eliminated or reduced to a level sufficient to treat the cachexia. As mentioned, Suzuki states that anti-IL-6R antibody blocked proliferation of myeloma cells, but not that myeloma cells already present could be eliminated or substantially eliminated from the body. Is simply arresting the proliferation of myeloma cells (as taught by Suzuki and Sato) enough to treat cachexia? According to Robbins, the answer is "no" because cachexia will continue to be caused by the cancer cells already present in the body (p. 295, left column). This conclusion becomes stronger when one considers that cachexia does not become apparent until cancer has advanced, so a medical practitioner would not begin to treat cachexia until there was a significant amount of cancer cells already present. Thus, the references collectively fail to teach one of ordinary skill in the art whether an anti-IL-6R

antibody has a strong enough effect on cancer at the advanced cachexia stage, such that it would reasonably be expected to have an appreciable effect on cachexia.

The References Collectively Fail To Give One A Reasonable Expectation Of Success That Cancer Can Be Treated In The First Place. Applicants submit herewith data showing that anti-IL-6R antibody does *not* inhibit colon 26 or occ-1 cancers. If one of ordinary skill in the art would not have reasonably expected to be able to treat cancer, then one could not have had a reasonable expectation of success in treating cancer cachexia.

Applicants Unexpectedly Discovered That Anti-IL-6R Antibody Treats Cachexia Even When It Does Not Treat Cancer And Despite Robbins' Suggestion That Cytokines Other Than IL-6 Mediate Cancer Cachexia. Perhaps what best illustrates the unobviousness of the presently claimed invention is applicants' demonstration that anti-IL-6R antibody treats cachexia even when it has no effect on the cancer causing the cachexia. This is particularly unexpected given that Robbins suggests TNF-alpha, IL-1, and/or IFN-gamma are primarily responsible for mediating cancer cachexia rather than IL-6R. At the time of the presently claimed invention, the prior art collectively taught away from the claimed approach to treating cachexia. Therefore, even if it would appear obvious to treat cachexia by treating the underlying cancer with anti-IL-6R antibody, the rejection would still be overcome by applicants' showing of unexpected results.

Accordingly, withdrawal of the rejection under 35 U.S.C. 103(a) is requested.

2. Disclosure of Related Application

Applicants wish to disclose a related application, which is Serial No. 08/875,927.

Conclusion

Applicants respectfully request entry of this proposed amendment. In light of the foregoing amendments and remarks, applicants submit that all claims are in condition for allowance, and they solicit an early indication to that effect. In the event that any issues

CPA of U.S. Serial No. 08/817,507

remain, the Examiner is invited to contact the undersigned at the telephone number listed below.

Respectfully submitted,

January 31, 2000
Date

Stephen B. Maebius
Reg. No. 35,264

FOLEY & LARDNER
Suite 500
3000 K Street, N.W.
Washington, DC 20007-5109
(202) 672-5300